et al. and Hogness *et al.* The specific grounds for rejection, and applicants' responses thereto, are set out in detail below.

II. Rejections Under 37 C.F.R. §112, Second Paragraph

Claims 1, 3-8 and 17-23 are rejected as indefinite. The specific rejections are dealt with below:

LXR expression construct: At the outset, applicants point out that the term "LXR expression construct" is not used in the claims.[1] Presumably, the examiner meant "LXRα expression construct." Moreover, applicants assume that the terms "expression construct" are not at issue but, rather, that the examiner believes "LXRα" is indefinite. Applicants traverse this assertion.

As the examiner has acknowledged, the LXRα gene was disclosed in the Willy *et al.* paper over a year prior to applicants' priority date. Thus, one of skill in the art would have been well apprised on what this term meant at the time the present application was filed. Indeed, as of the time the Willy *et al.* paper was published, the field was regularly using this term. *See* Leblanc & Stunnenberg, "9-Cis retinoic acid signaling: Changing partners causes some excitement," *Genes Dev.* 9, 1811-1816, 1995.

LXR protein: Again, the examiner has acknowledged that the LXRα protein sequence was disclosed in the Willy *et al.* paper over a year prior to applicants' priority date. Thus, again, applicants submit that since Willy *et al.* describe the LXRα protein by providing

[1] This is true with one exception, in claim 20, which now has been corrected.

an amino acid sequence, one of skill in the art was well aware of what this term meant at the time the present application was filed.

Oxysterol activator: The examiner argues that this term is not defined or limited by structure. Both of these statements are incorrect. First, an oxysterol is a well-defined chemical term that literally means "oxygenated sterol." *See* Gibbons, G.F., "The role of oxysterols in the regulation of cholesterol biosynthesis," *Biochem. Soc. Trans.* 11, 649-651, 1983; and Parish *et al.*, "Oxysterols: chemical synthesis, biosynthesis, and biological activities," *Lipids* 21, 27-30, 1986. Second, the specification provides a number of examples of what this term means such that if there were doubt about the "metes and bounds" of this term, the examples would provide clarification. See specification at page 5, lines 17-23. And third, the specification references an article by Russell (C25) that further characterizes this class of compounds. Specification at page 4, lines 11-13. Together, this evidence refutes the examiner's position.

In sum, none of the terms objected to by the examiner are indefinite when viewing the prior and the specification as a whole. Reconsideration and withdrawal of the rejection is, therefore, respectfully requested.

III. Rejection Under 37 C.F.R. §112, First Paragraph

Claims 1, 3-8 and 17-23 are rejected as lacking an enabling disclosure. The examiner argues again that the term "LXR" is so broad as to encompass mutants and variants that are incapable of function. Applicants traverse.

Again, applicants respectfully point out that the term LXR is not used in the claims – the term at issue is LXRα.[2] Further, given the disclosure of Willy *et al.*, applicants submit that the examiner is incorrect in asserting that the term is defined only by function. One of skill in the art would not, as argued by the examiner, be forced to conduct undue experimentation to identify an LXRα molecule that functions in accordance with the present invention. Rather, one is provided with clear instruction as to what ***is*** operable, and the claims only reach that with ***is*** operable. It is not the function of the claims, however, to specifically exclude possible inoperative substances. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 USPQ 409 (Fed. Cir. 1984). And where applicants have limited the scope of the claims to the area where utility has not been properly challenged, maintenance of the rejection is improper. *In re Frillette*, 165 USPQ 259 (CCPA 1970); *In re Buting*, 163 USPQ 689 (CCPA 1969). Should one of skill in the art choose to modify the LXRα molecule of Willy *et al.*, it is always possible that an inoperative molecule would be created. However, since the claims do not encompass such inoperable species, no issue of enablement is created by such a scenario.

The examiner also argues that deposit is required for the constructs of claims 3, 6 and 19. The claims have been canceled without prejudice. Reconsideration and withdrawal of the rejection/requirement is respectfully requested.

IV. Rejections Under 37 C.F.R. §102

A. Willy et al. - §102(b)

The examiner has rejected all claims as anticipated by Willy *et al.* The examiner correctly identifies the reference as disclosing the LXRα gene and protein sequences. However,

[2] See footnote 1.

the examiner then incorrectly states that the various candidate ligands screened by Willy *et al.* qualify as "oxysterol activators." Thus, applicants traverse the rejection.

As with the rejections advanced above, the examiner is arguing that the terms are so broad as to capture subject matter that clearly is distinct. Unlike the other anticipation rejection (below), the examiner has at least identified the correct gene – LXRα. However, the retinoids used in the Willy *et al.* screens cannot, under any stretch of the imagination, be viewed as an oxysterol. For this reason alone, the rejection falls. Reconsideration and withdrawal of the rejection is, therefore, respectfully requested.

B. Hogness et al. - §102(e)

The examiner also argues that all claims are anticipated by Hogness *et al.* The entire basis for this rejection appears to be the allegation that the terms "LXR expression construct," "LXRα protein" and "oxysterol activator" are so broad that they can encompass a protein so disparate as the ecdysteroid receptor disclosed by Hogness *et al.* Applicants traverse.

Again, applicants point out that the term "LXR expression construct" is not found in the claims – the term is now "LXRα expression construct."[3] Moreover, the examiner is ignoring clear evidence in the form of Willy *et al.* that defines what an LXRα expression construct and protein are. In light of Willy *et al.*, it simply is not credible to argue that one would confuse LXRα with the ecdysteroid receptor.

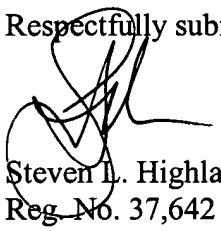
Thus, for many of the reasons indicated above, the instant claims are distinguishable from the Hogness *et al.* patent. Reconsideration and withdrawal of the rejection is respectfully requested.

[3] See footnote 1.

V. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,



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Date: October 2, 2002

APPENDIX A: MARKED UP COPY OF CLAIMS

3. (Canceled) The method of claim 1, wherein said LXRα expression construct is selected from the group consisting of CMX-LXRα, CMX-GAL4-LXRα and A5C-LXRα.

6. (Canceled) The method of claim 1, wherein said reporter construct is selected from the group consisting of TK-LXRE-LUC, TK-LXRE-CAT, ADH-LXRE-LUC, ADH-LXRE-CAT, TK-gal4$_{uas}$-LUC and TK-gal4$_{uas}$-CAT.

19. (Canceled) The method of claim 1, wherein said reporter construct is selected from the group consisting of TK-MH100x4-LUC, TK-LXREx3-LUC and ADH-LXREx2-LUC.

20. (Amended) A method of screening for an oxysterol that activates LXRα mediated transcription, comprising the steps of:

(a) providing a host cell comprising a reporter construct and an LXRα expression construct, wherein transcription of said reporter construct is activated when an oxysterol activator of LXRα binds to the LXRα protein;

(b) treating the host cell with a candidate oxysterol activator of LXRα mediated transcription; and

(c) determining whether said oxysterol activates LXRα mediated transcription of said reporter construct,

wherein activation of reporter construct transcription indicates that said oxysterol is an activator of LXRα mediated transcription.